
Notch activity modulates the responsiveness of neural progenitors to sonic hedgehog signaling.

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Public Summary:

Our study shows how a signalling factor called Notch helps control where nerve stem cells go in the spinal cord in order to set up a functional peripheral nervous system.

Scientific Abstract:

Throughout the developing nervous system, neural stem and progenitor cells give rise to diverse classes of neurons and glia in a spatially and temporally coordinated manner. In the ventral spinal cord, much of this diversity emerges through the morphogen actions of Sonic hedgehog (Shh). Interpretation of the Shh gradient depends on both the amount of ligand and duration of exposure, but the mechanisms permitting prolonged responses to Shh are not well understood. We demonstrate that Notch signaling plays an essential role in this process, enabling neural progenitors to attain sufficiently high levels of Shh pathway activity needed to direct the ventral-most cell fates. Notch activity regulates subcellular localization of the Shh receptor Patched1, gating the translocation of the key effector Smoothened to primary cilia and its downstream signaling activities. These data reveal an unexpected role for Notch shaping the interpretation of the Shh morphogen gradient and influencing cell fate determination.

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